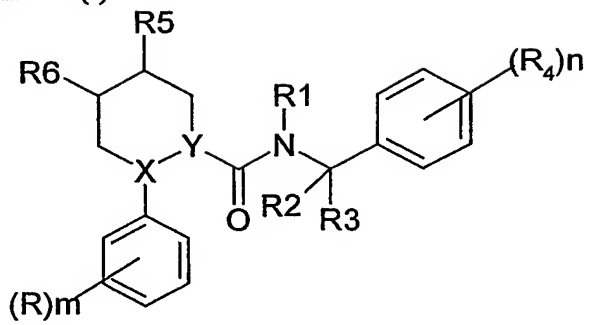
Claims

1. A compound of formula (I)



(I)

wherein:

R represents halogen or C_{1-4} alkyl;

R_1 represents hydrogen or C_{1-4} alkyl;

R_2 represents hydrogen , C_{1-4} alkyl or R_2 together with R_3 represents C_{3-7} cycloalkyl;

R_3 represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl or C_{3-6} alkenyl; or R_1 and R_3 together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group;

R_4 represents trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy or halogen;

R_5 is hydrogen and R_6 is NR_7R_8 or R_5 is NR_8R_9 and R_6 is hydrogen;

R_7 represents hydrogen or C_{1-4} alkyl or R_7 and R_8 together with nitrogen to which they are attached are a saturated 5 to 7 membered heterocyclic group containing oxygen;

R_8 represents hydrogen, phenyl, C_{3-7} cycloalkyl, $(CH2)pC(O)NR_{10}R_{11}$, a saturated 5 to 7 membered heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen and optionally substituted by C_{1-4} alkyl, $S(O)_2C_{1-4}$ alkyl or C(O) C_{1-4} alkyl, a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen and optionally substituted by C_{1-4} alkyl $S(O)_2C_{1-4}$ alkyl or C(O) C_{1-4} alkyl or R_8 represents a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms and optionally substituted by C_{1-4} alkyl, $S(O)_2C_{1-4}$ alkyl or C(O) C_{1-4} alkyl; or R_8 is a C_{1-6} alkyl group optionally substituted by one or two groups selected from fluorine, phenyl(optionally substituted by C_{1-4} alkyl, C(O) C_{1-4} alkyl or halogen), =O, C_{3-7} cycloalkyl, hydroxy, amino, dimethylamino, aminocarbonyl, C_{1-4} alkoxy or trifluoromethyl;

R_9 is hydrogen, C_{1-4} alkyl or R_9 and R_8 together with nitrogen to which they are attached are a 5 to 7 membered heterocyclic group optionally containing another heroatom selected from oxygen, sulphur and nitrogen and optionally substituted by one or two groups selected from C_{1-4} alkyl, =O, $S(O)_2C_{1-4}$ alkyl, C(O) C_{3-7} cycloalkyl or C(O) C_{1-4} alkyl;

R_{10} and R_{11} are independently hydrogen or C_{1-4} alkyl group;

X represents a nitrogen atom and Y is CH or X represents CH and Y is nitrogen;

m is zero or an integer from 1 to 3;

n is an integer from 1 to 3;

p is zero, 1 or 2;

and pharmaceutically acceptable salts and solvates thereof.

2. A compound as claimed in claim 1 wherein R_6 is NR_7R_8 and R_5 is hydrogen, Y is nitrogen and X is CH or wherein R_6 is hydrogen and R_5 is NR_8R_9, Y is CH and X is nitrogen.

3. A compound as claimed in claim 1 or claim 2 wherein R is a halogen (e.g. fluorine) and/or a C_{1-4} alkyl (e.g. methyl) group and m is zero or an integer from 1 to 2.

4. A compound as claimed in any claims from 1 to 3 wherein R_1 is a methyl group.

5. A compound as claimed in any claims from 1 to 4 wherein R_2 is a hydrogen atom or a methyl group.

6. A compound as claimed in any claims from 1 to 5 wherein R_3 is a hydrogen atom or a methyl group.

7. A compound as claimed in any claims from 1 to 6 wherein R_4 is a trifluoromethyl group and/or halogen (i.e chlorine) and n is 2.

8. A compound as claimed in any claims from 1 to 7 wherein R_5 is hydrogen, $NH(C_{3-7}$ cycloalkyl),$NH(C_{1-4}$alkylC_{3-7} cycloalkyl), 1-piperazinyl(optionally substituted by one or two groups selected from C_{1-4} alkyl, =O, $S(O)_2C_{1-4}$ alkyl, C(O) C_{3-7} cycloalkyl or C(O) C_{1-4} alkyl); piperidyl (optionally substituted by one or two groups selected from C_{1-4} alkyl, =O,) or morpholino.

9. A compound as claimed in any claims from 1 to 8 wherein R_6 is hydrogen, $N(C_{1-6}alkyl)_2$, $NH(C_{1-6}alkyl)$, $NH(CH_2)pC(O)NR_{10}R_{11}$ wherein p is 1 or 2 and R_9 and R_{10} are independently hydrogen or methyl, $NH(C_{1-6}$ alkyltrifluoromethyl), $NH(C_{1-6}alkylC_{1-4}alkoxy)$, $NH(C_{1-6}alkylfluorine)$, $N(C_{1-6}$ alkyl)$(C_{1-6}$ alkylfluorine), $NH(C_{1-6}$ alkylphenyl), $NH(C_{3-7}cycloalkyl)$, NH(piperidyl), NH (C_{1-6} alkyl aminocarbonyl), $NH(C_{1-6}$ alkyl-1.3 dioxolan-yl) or morpholino.

10. A compound as claimed in any claims from 1 to 9 wherein
R_6 is NR_7R_8 and R_5 is hydrogen, Y is nitrogen and X is CH or wherein R_6 is hydrogen and R_5 is NR_8R_9, Y is CH and X is nitrogen;
R_7 is hydrogen or methyl;
R_8 is methyl, ethyl, dimethylpropyl, cyclopropyl, cyclobutyl, $CH_2C(O)NH_2$, piperidinyl, 1-methyl-piperidinyl, methyl substituted by a group selected from phenyl, cyclopropyl, 4-acetyl-piperazino, fluorine, methoxy, trifluoromethyl and 1.3 dioxolan-yl;
R_9 is hydrogen or methyl;
R_9 and R_8 together with nitrogen to which they are attached is 1-piperazinyl, acetyl-1-piperazinyl, morpholino;
R_7 and R_8 together with nitrogen to which they are attached is morpholino;
R is independently fluorine or methyl;

R_4 is trifluoromethyl and/or chlorine;
m is 1 or 2;
n is 2.

11. A compound as claimed in any claims from 1 to 10 selected from :
4-(S)-Dimethylamino-2-(R)-(4-fluoro-2-methyl-phenyl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride;
4-(S)-Dimethylamino-2-(R)-(4-fluoro-2-methyl-phenyl)-piperidine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide hydrochloride;
4-(S)-(2-Fluoroethyl)-amino-2-(R)-(4-fluoro-2-methyl-phenyl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis)-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride;
4-(S)-(2-Fluoro-ethylamino)-2-(R)-(4-fluoro-2-methyl-phenyl)-piperidine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide hydrochloride.

12. A compound as claimed in any claims from 1 to 11 for use in therapy.

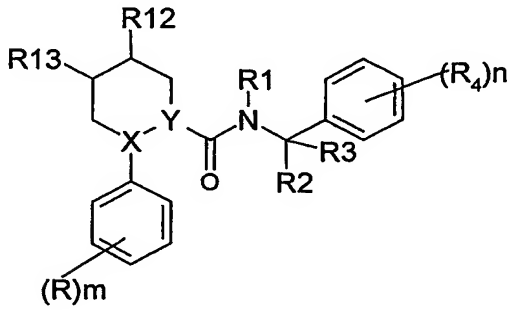
13. The use of a compound as claimed in any claims from 1 to 11 in the preparation of a medicament for use in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins.

14. The use of a compound as claimed in any claims from 1 to 11 in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins.

15. A pharmaceutical composition comprising a compound as claimed in any claims from 1 to 11 in a mixture with one or more pharmaceutically acceptable carriers or excipients.

16. A method for the treatment of a mammal, including man, in particular in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins, comprising administration of an effective amount of a compound as claimed in any claims from 1 to 11.

17. A process for the preparation of a compound as claimed in any claims from 1 to 11 by reductive N-alkylation of a compound of formula (II), wherein R_{12} is =O and R_{13} is hydrogen or R_{12} is hydrogen and R_{13} is =O



(II)

NR_5R_6

(III)

with an amine derivative (III) or salts thereof in the presence of a suitable metal reducing agent, followed where necessary or desired by one or more of the following steps:

i) removal of any protecting group;

ii) isolation of the compound as a salt or a solvate thereof;

separation of a compound of formula (I) or derivative thereof into the enantiomers thereof.